ITW

PATENT
Attorney Docket No. 09963.0008
Application No.: 10/571,991
Customer No. 22,852

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In Re Application of:	)	
	)	
Robert Hugh Bradbury et al.	)	Group Art Unit: 4161
	)	
Application No.: 10/571,991	)	Examiner: D. Willis
	)	
Filed: March 15, 2006	)	
	)	
For: QUINAZOLINE DERIVATIVES	)	

Mail Stop PGPUB
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

REQUEST FOR CORRECTION OF PUBLISHED APPLICATION UNDER 37 C.F.R. § 1.221(b)

On April 24, 2008, the Office published the above identified Application No. 10/571,991 as Publication No. US-2008-0096881-A1. The published application contains a material mistake that is the fault of the Office. Attached hereto is a copy of the page of the originally filed application and a marked-up copy of the corresponding page of the published application containing the mistake. The mistake, which is indicated in red ink on the marked-up copy of the published application, is as follows:

Paragraph 0304, line 3, Formula IV by a Mitsunobu reaction with $R^1O_2C(CH_2)_n$)-

A mistake is material when it affects the public's ability to appreciate the technical disclosure of the patent application publication or determine the scope of the provisional rights that an applicant may seek to enforce upon issuance of a patent. *See* CFR § 1.221(b).

The mistake in the formula in Paragraph 0304 is that the subscript is "n" whereas the remainder of that Paragraph refers to "m". Thus, the mistake is material as it may affect the public's ability to appreciate the technical disclosure of the patent application publication. Finally, a margin of error can be of relevance to the anticipatory value of a reference. For at least these reasons, the mistake is material and accordingly should be corrected.

For all of these reasons, Applicants request that the Office correct the mistake in the published application, and forward to Applicants a copy of the corrected published application once it has been corrected.

Applicants believe that no petition or fee is due in connection with this Request. However, if any petition or fee is due, please grant the petition and charge the fee to our Deposit Account No. 06-0916.

Respectfully submitted,

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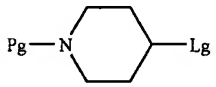
DATE: June 24, 2008

[0290] Reaction Scheme 2 may be generalised by the skilled man to apply to compounds within the present specification which are not specifically illustrated (for example to introduce a substituent other than methoxy at the 7-position in the quinazoline ring).

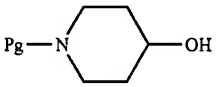
[0291] Compounds of the Formula III are commercially available or may be prepared using standard techniques, for example as illustrated in U.S. Pat. No. 5,252,586 and WO 94/27965.

[0292] Compounds of the Formula IV may be prepared by reaction of a compound of Formula II with a compound of XVa or XVb:

XVa



XVb



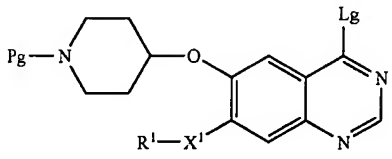
wherein Lg is a displaceable group as hereinbefore defined and Pg is a suitable protecting group. For example, Lg may be an alkanesulfonyloxy group, such as methanesulfonyloxy and Pg may be tert-butylcarboxylate.

[0293] The reaction of the compound of Formula II with the compound of Formula XVa may be carried out using analogous conditions to those described in process (a) above, followed by removal of the protecting group under standard conditions. For example, the reaction may be carried out using potassium carbonate as a suitable base, N-methylpyrrolidin-2-one as a suitable diluent and at a temperature of about 105° C.

[0294] The reaction of the compound of Formula II with the compound of Formula XVb may be carried out under Mitsunobu conditions as described in process (e) above, followed by removal of the protecting group under standard conditions.

[0295] Compounds of the Formula IV may also be prepared by reaction of a compound of the Formula IX with a compound of the Formula XVc:

XVc



wherein Lg, X^1 and R^1 are as hereinbefore defined and Pg is a suitable protecting group.

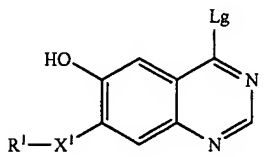
[0296] The reaction of the compound of Formula IX with the compound of Formula XVc may be carried out using analogous conditions to those described in process (j) above, followed by removal of the protecting group under standard conditions.

[0297] Compounds of the Formula VI may be prepared using process (a) or process (e) above, starting with a compound prepared, for example using reaction scheme 1.

[0298] Compounds of the Formula VII may be prepared using, for example, process (a) or process (d) or process (e) in which the group represented by R^1 is appropriately functionalised with a suitable displaceable group Lg such as chloro or bromo.

[0299] Compounds of the Formula VIII may be prepared using conventional methods well known in the art. For example the hydroxy protecting group, Pg, in a compound of the Formula XI as hereinbefore described in Reaction Scheme 1 is removed to give the compound of the Formula XIII:

XIII



The protecting group Pg may be removed from the compound of Formula XI using conventional techniques.

[0300] The compound of the Formula XIII may then be coupled with a compound of the Formula III as hereinbefore defined using analogous conditions to those described in process (a) or process (e).

[0301] Compounds of the Formula XX may be prepared, for example, using process (a), process (c) or process (k) above.

[0302] Compounds of the Formula V, V' and IX are commercially available or may be prepared using standard techniques. Compounds of the Formula V" may be prepared using standard techniques, for example as illustrated in Synthesis, 1993, 12, 1233 and Tetrahedron, 1992, 48, 5557.

[0303] Compounds of the Formula X where m is 1, 2 or 3 may, for example, be prepared from a compound of the Formula IV by alkylation with $R^1O_2C(CH_2)_m$-Lg, wherein Lg and R^1 are as hereinbefore defined, in the presence of a base and using analogous conditions to those described in process (c) above, followed by transformation of the ester to the carboxylic acid (for example by saponification or acidic deprotection).

[0304] Alternatively, compounds of the Formula X where m is 1, 2 or 3 may be prepared from a compound of the Formula IV by a Mitsunobu reaction with $R^1O_2C(CH_2)_m$-OH using analogous conditions to those described in process (e) above, followed by transformation of the ester to the carboxylic acid (for example by saponification or acidic deprotection).

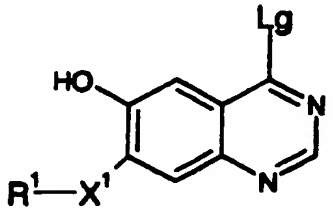
[0305] Certain novel intermediates utilised in the above processes are provided as a further feature of the present invention together with the process for their preparation.

[0306] According to a further feature of the present invention there is provided the compounds of the Formulae VI, VII, VIII, X and XX or a salt thereof, (including pharmaceutically acceptable salts thereof), as hereinbefore defined. Examples of such compounds are 6-{[1-(N-(2-chloroethyl) carbamoyl)piperidin-4-yl]oxy}-4-(3-chloro-2-fluoroanilino)-7-methoxyquinazoline, [4-({4-(3-chloro-2-fluoroanilino)-7-methoxyquinazolin-6-yl}oxy)piperidin-1-yl]

Compounds of the Formula VI may be prepared using process (a) or process (e) above, starting with a compound prepared, for example using reaction scheme 1.

Compounds of the Formula VII may be prepared using, for example, process (a) or process (d) or process (e) in which the group represented by R^1 is appropriately functionalised with a suitable displaceable group Lg such as chloro or bromo.

Compounds of the Formula VIII may be prepared using conventional methods well known in the art. For example the hydroxy protecting group, Pg, in a compound of the Formula XI as hereinbefore described in Reaction Scheme 1 is removed to give the compound of the Formula XIII:



XIII

The protecting group Pg may be removed from the compound of Formula XI using conventional techniques.

The compound of the Formula XIII may then be coupled with a compound of the Formula III as hereinbefore defined using analogous conditions to those described in process (a) or process (e).

Compounds of the Formula XX may be prepared, for example, using process (a), process (c) or process (k) above.

Compounds of the Formula V, V' and IX are commercially available or may be prepared using standard techniques. Compounds of the Formula V'' may be prepared using standard techniques, for example as illustrated in Synthesis, 1993, *12*, 1233 and Tetrahedron, 1992, *48*, 5557.

Compounds of the Formula X where m is 1, 2 or 3 may, for example, be prepared from a compound of the Formula IV by alkylation with $R^1O_2C(CH_2)_m$-Lg, wherein Lg and R^1 are as hereinbefore defined, in the presence of a base and using analogous conditions to those described in process (c) above, followed by transformation of the ester to the carboxylic acid (for example by saponification or acidic deprotection).

Alternatively, compounds of the Formula X where m is 1, 2 or 3 may be prepared from a compound of the Formula IV by a Mitsunobu reaction with $R^1O_2C(CH_2)_m$-OH using